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Impact of COVID-19 Pandemic on Antimicrobial Resistance: A Review of Trends and Antibiotic Patterns in India

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Abstract

The pandemic situation caused by SARS-CoV2 had a severe influence on the health system all over the world. After two and half years of this situation, the WHO has downgraded the COVID-19 pandemic and has declared that it is no longer a global health threat. Though the COVID-19 infection has reduced around the world, the irrational intake of antibiotics for the past 3 years has aggravated the antimicrobial resistance (AMR) globally. In this review, we examined the pattern of reported AMR during the pandemic in India and also highlighted antibiotic susceptibility during the pandemic situation. An online search was carried out to include all the original articles that were published in India on antimicrobial resistance and COVID-19 from March 2020 to May 2023 in the following databases: PUBMED, SCOPUS, EMBASE, Cochrane, Web of Science, and Google Scholar; Key antimicrobial-resistant findings were identified from 12 relevant studies. Among the gram-negative bacteria, the prevalent antimicrobial-resistant bacteria were A. baumanii and K. pneumonia followed by E. coli. The predominant resistant gram-positive bacteria were S. aureus. Around 50% of the Acinetobacter spp were carbapenem-resistant. Multidrug-resistant K. pneumonia, A. baumannii and E. coli were also reported. Increased intake of antibiotics during the COVID-19 pandemic may have increased the virulence of the superbug by showing resistance to various drugs. Judicious use of antibiotics, public awareness campaigns on antibiotic usage, and improved hygiene practices, both in healthcare settings and in the community can help in reducing the transmission of infections and subsequently decreasing antimicrobial resistance.

Keywords: *Antimicrobial Resistance, COVID-19, Antibiotic Patterns, Multidrug-Resistant Strains, Online Search.*

Introduction

The pandemic situation caused by the Coronavirus disease of 2019 (COVID-19) posed various challenges to the healthcare system globally. In the year 2020 on March 11ththe World Health Organization (WHO) declared the pandemic situation officially declared that there is a pandemic situation which was caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Measures such as social distancing, quarantines, mask-wearing, and regular hand washing became standard practices for preventing and managing COVID-19. Numerous countries experienced disruptions in health services, often halting all healthcare activities starting from the initial days of the pandemic. However, after two and half years of the pandemic period, the WHO has downgraded the COVID-19 pandemic and has declared that it is no longer a global health

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threat. Globally, as of 31st June 4th2024, there have been 775, 522, 404 positive cases of COVID-19 and in India approximately 45 million cases have been reported [1].

Difficult-to-treat bacterial infections have been growing in India even before the COVID-19 era. India is known to supply cost-effective and affordable medicines and vaccines to the whole world. In the years 2020 and 2021, admissions to all the hospitals had increased dramatically due to Covid-19. The use of anti-parasite, anti-viral, anti-bacterial and the utilization of anti-inflammatory medications to avoid secondary infections in COVID-19 patients during an extended pandemic posed a risk of future complications, notably exacerbating antimicrobial resistance (AMR) [2]. There was a four-fold increase in the number of patients taking antimicrobials in 2021 compared to 2019 [3]. There was increased use and misuse of antibiotics and other medications for effective therapeutic regimens for COVID-19 treatment [4]. Improper use of antibiotics may have led to a surge in antimicrobial resistance. This may also result in an increased diversity of antimicrobial gene reservoirs and therefore these pathogens will no longer respond to the common antibiotics. It's going to be a big challenge for the doctors in various intensive care units (ICU) to treat infections in critically ill patients.

In India, an estimated 216 million excess doses of antibiotics were consumed between June and September 2020 alone [5]. Overprescribing of antibiotics is still a reality and there is very little guidance for prescribing antibiotics. Added to this, broad-spectrum antibiotics were sold over the counter. These resulted in increased antimicrobial resistance, increased cost of treatment, increased infections, and increased hospital stay days. A retrospective observational study in Maharashtra analyzed the prescription patterns among COVID-19 patients and found that over 80% were prescribed antibiotics. Interestingly, the study revealed that the duration of hospital stays was comparable between patients who received antibiotics and those who did not [6]. Globally there was an increase in the consumption of antibiotics during the pandemic which may have given rise to deadly resistant microorganisms that are difficult to treat. A study from Brazil demonstrated that multidrug-resistant gram-negative bacterial infection associated with COVID-19 had increased mortality rates [7]. This challenge was exacerbated by inadequate waste management infrastructure and poor sanitation conditions prevalent in developing countries. The accumulation of antimicrobial residues in the environment can contribute to the development of antibiotic resistance in bacteria [8]. Therefore, it is no wonder that antimicrobial resistance is called the invisible or the silent pandemic.

A retrospective study was done in ten hospitals that are part of the Indian Council of Medical Research (ICMR) AMR surveillance network, looking at secondary infections in COVID-19 patients who were admitted to wards and intensive care units (ICUs) between June and August 2020. The investigation revealed that patients with secondary infections showed a mortality rate of 56.7%, contrasting with the overall mortality rate of 10.6% among all admitted COVID-19 patients. Gram-negative bacteria were identified in 78% of cases, with *Klebsiella pneumoniae* (29%) and *Acinetobacter baumannii* (21%) being the most prevalent. Additionally, 35% of patients reported polymicrobial infections, including fungal infections. A significant proportion of *A. baumannii* (92.6%) and *K. pneumoniae* (72.8%) exhibited high levels of carbapenem [9] resistance as shown in Fig. 1. The purpose of this review was to investigate how COVID-19 affected AMR. To that end, we looked at the pattern of AMR cases that were reported during the pandemic and emphasized

antibiotic susceptibility during the COVID-19 pandemic in India.

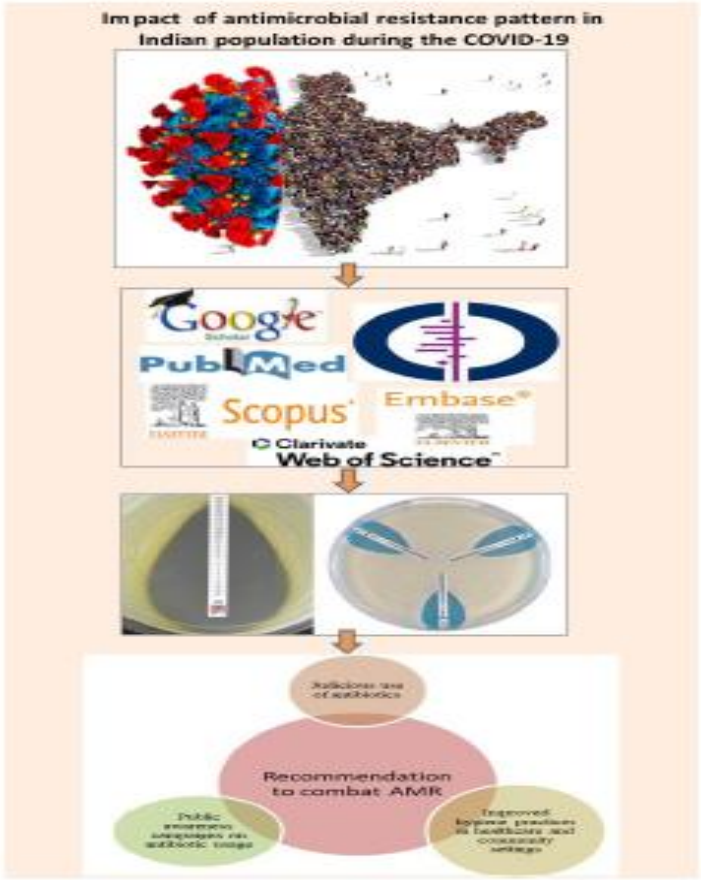

Figure 1. Schematic Representation of Antimicrobial Resistance (AMR) Patterns during the COVID-19 Periods in India

Material and Methods

An online search was carried out to include all the original articles that were published in India on antimicrobial resistance and COVID-19 from March 2020 to May 2023. The article search was carried out from the following databases: PUBMED, SCOPUS, EMBASE, Cochrane, Web of Science, and Google Scholar. Only those articles with full text and in English language were chosen. Studies that reported on antimicrobial resistance and antibiotic susceptibility and COVID-19 were included. The terms that were used in the search strategy were “antimicrobial resistance”, “COVID-19”, “SARS CoV-2”, “antibacterial" and “antibiotics susceptibility”. Using Boolean operators (AND/OR) the following terms were searched: “antimicrobial resistance and COVID-19”, “antimicrobial resistance and COVID-19 pandemic”, “antibiotic sensitivity or antibiotic resistance”, “antibiotic sensitivity and COVID-19”, “antibiotic resistance and COVID-19”. Editorials, case reports, perspectives, viewpoints, systematic reviews and letters to the editor, non-English language articles, and non-human studies were all excluded. The full-text screening was done by the authors. Analysis of each study was narrated using relevant data.

Results

The search identified 12 relevant studies from the various databases. Six of them were retrospective studies and 6 were prospective studies. Four studies were from Delhi, two from Tamil Nadu, Karnataka, and Rajasthan, and one study from Odisha and Telangana. Key antimicrobial-resistant findings are tabulated in Table 1. In 9 studies, clinical

isolates/blood samples were from COVID-19-positive patients [10-15]. The number of COVID-19-positive patients ranged from 56-1578. Their clinical isolates/blood samples ranged from 86-290. In the rest of the studies, clinical isolates/blood samples ranged from 395-13747. Two studies reported the secondary infections and AR findings from the intensive care unit (ICU) [16, 17] and one study was from both ICU and wards [11]. A retrospective observational study compared blood culture results during the first wave of the COVID-19 pandemic (April 2020 to September 2020) with those during the second wave (April 2021 to September 2021) [17].

Table 1. Summary of the Key Antimicrobial-Resistant (AMR) Findings of 12 Studies from India

Authors (year)	**State**	**Study design & duration**	**Sample characteristics**	**Key Antimicrobial Resistant (AMR) findings**	**References**
Juliana A (2022)	Chennai, Tamil Nadu	One-year retrospective study	86 GNB* isolates and 59 GPB† isolates from 145 COVID-19 positive patients.	The main GNB organisms detected were *K. pneumoniae*, with *P. aeruginosa*, *Acinetobacter spp*., and *E. coli* following. *K. pneumoniae* isolates exhibited a high resistance rate, while *P. aeruginosa* showed the highest sensitivity. More than half of *Acinetobacte*r spp. were carbapenem-resistant, and 80% of *K. pneumoniae* were resistant to third-generation cephalosporins.	[10]
Rajni E et al (2021)	Jaipur, Rajasthan	Retrospective observational study of 5 months	158 blood culture samples from 1578 COVID-19 positive patients (ICU and wards)	Approximately 9.4% of cases exhibited positive blood cultures, with 90% of gram-positive isolates demonstrating methicillin resistance. There was a notable high level (70–90%) of resistance observed for macrolides, clindamycin, and quinolones, although susceptibility was retained for gentamicin, cotrimoxazole, vancomycin, linezolid, and daptomycin. Among gram-negative isolates, *P. aeruginosa* displayed sensitivity to all drugs except ticarcillin, while *E. coli* exhibited multidrug resistance and sensitivity limited to tigecycline and colistin.	[11]
Khurana S et al (2021)	New Delhi	Prospective study of three months	290 clinical isolates from 151 COVID-19 positive patients	Among 96 bacterial isolates, *K. pneumoniae* (33.3%), followed by *A. baumannii* (27.1%), *E. coli* (16.7%), and *P. aeruginosa* (11.5%). CoNS‡ was identified in 12 out of 19 positive blood cultures. Overall resistance rates varied from 9% to 84% across all organisms studied. Resistance to third-generation cephalosporins and carbapenems ranged from 64% to 69%. Notably, all isolates demonstrated sensitivity to colistin.	[12]
Bhaskaran S (2022)	Chennai, Tamil Nadu	Retrospective study -3	56 COVID-19 positive patients	Out of 56 patients, 12 (21.4%) were identified as having bacterial	[13]

		months		infections. Among the GNB isolated, 22.2% exhibited MBL[§] production, while 55.5% showed ESBL[¶] production. Additionally, out of all the organisms isolated, 9 were classified as multidrug-resistant, accounting for 81.8% of cases.	
Palanisamy N et al (2021)	Jodhpur, Rajasthan	Retrospective observational study of 17 months	750 ICU COVID-19 positive patients (BSI)	64 (8.5%) patients developed BSI. Around 82.8% had GNB. *A. baumannii* was the commonest isolate (32.8%), followed by *K. pneumoniae* (21.9%). Multidrug-resistant organisms were identified in 57.8% of the cases, with a predominant presence in the *K. pneumoniae* and *Enterococcus* groups. Approximately 47.2% of GNBs were resistant to carbapenems.	[14]
Boorgula S Y (2022)	Hyderabad, Telangana	Retrospective study of 2 months	200 clinical samples were obtained from 122 COVID-19-positive patients.	*K. pneumoniae* (n = 68) was the most frequently isolated pathogen, followed by *A. baumannii* (n = 54), with an overall increase of 6% in carbapenem resistance observed among the isolates.	[15]
Raksha K (2021)	Bengaluru, Karnataka	Prospective study of 3 months	123 ICU COVID-19 positive patients	Among mechanically ventilated patients, 47% developed multidrug-resistant *K. pneumonia infections*. Approximately 26% of patients with central lines developed central line-associated bloodstream infections (CLABSI), primarily caused by CoNS followed by multi-drug-resistant *K. pneumoniae*. In catheterized patients, 51% developed catheter-associated urinary tract infections (CAUTI), with MDR *K. pneumoniae* and *A. baumannii.*	[16]
Saini V et al (2022)	New Delhi	Retrospective observational study of 5 months in 2020 (first wave) and 5 months in 2021 (second wave).	1470 (1stwave) and 4200 (2nd wave) blood culture samples (BSI) from COVID-19 positive patients.	In the 1st wave, CoNS was 32.8% followed by *S. aureus* (29.7%) in which 60.3% were MRSA**K. Pneumonia* and *E. coli* were the most isolated GNB. In the 2nd wave, *S. aureus*(48.9%) in which 55% of them were MRSA. In GNB, *K. pneumonia was* 11.8% followed by *A. baumannii*(10.8%) and *E. coli* (7%). Gram-positive isolates were susceptible to aminoglycosides, macrolides, fluoroquinolones and cotrimoxazole. Vancomycin and linezolid were found 100% susceptible to gram-positive cocci	[17]
Sreenath et al., 2021	New Delhi	June 2020 to January 2021	191 COVID-19 patients	Bacterial coinfections were detected in 79% of the patients, with *S. aureus* being the predominant bacterium, followed by *K. pneumoniae*. Among these coinfections, both *A. baumannii* and *K. pneumoniae* were found in five	[18]

				patients.	
Saxena S et al (2023)	New Delhi	Prospective study of 12 months	5792 bacterial isolates out of 46, 629 specimens	The most common bacterial isolates were *E. coli* (30%), *S. aureus* (21%), *K. pneumonia* (18%), *P. aeruginosa*(10%), *A.baumanii*(8%) and *Enterococcus sp.* (5%). Less than 50% of *Acinetobacter sp.* were carbapenem susceptible. A high rate of MRSA (74%) was observed.	[19]
Sarathi et al (2023)	Bhuvaneshwar, Odisha	Prospective, cross-sectional study of 16 months	13,747 blood samples.	14% were culture positive. Around 15% were NFGNB†† and 29% were multi-drug resistant *Elizabethkingia* spp. Over 75% exhibited resistance to carbapenems, aminoglycosides, as well as third- and fourth-generation cephalosporins.	[20]
Dhar E et al (2023)	Mysuru, Karnataka	Prospective study	395 *S. aureus isolates*.	62% of isolates were identified as MRSA. The MRSA were highly susceptible (63%-100%) to linezolid, vancomycin, daptomycin, oxacillin, trimethoprim/sulfamethoxazole, levofloxacin, ciprofloxacin, clindamycin and erythromycin.	[21]

*GNB-Gram Negative Bacteria, †GPB-Gram Positive Bacteria, ‡CoNS- Coagulase Negative *Staphylococcus*, §MBL-Mettalo β Lactamases, ¶ESBL-Extended spectrum β Lactamases, **MRSA- Methicillin Resistant *Staphylococcus aureus,* ††NFGNB-Non Fermenting Gram Negative Bacteria.

Nature of Antimicrobial Resistant Bacteria during COVID-19

During the COVID-19 pandemic surge, multidrug-resistant *K. pneumoniae* and *A. baumannii* were prevalent pathogens among gram-negative microorganisms [14-17].The majority (73%) of the studies had reported the presence of *A. baumannii* in the clinical sample the ranging from 8% to 32% [17-19]. In one study, it was observed only during the second wave of pandemic where the commonest isolated bacteria were *K. Pneumoniae* followed by *A. baumannii* [17]. Over 50% of *Acinetobacter* spp was carbapenem-resistant in two studies [10, 19]. In COVID-19-positive patients, *A. baumannii* and *K. pneumoniae* were the most common organisms isolated from bloodstream infections (BSI) [14]. A study in New Delhi reported, that four patients were identified for *A. baumanii* coinfections in the COVID-19 ward, among the four isolates three were resistant to all tested antibiotics except colistin and one isolate showed susceptibility to colistin and a combination of cefoperazone/sulbactam. *K. pneumonia* isolated from one patient showed susceptibility to all the antibiotics used in the study [18]. The secondary infections were significantly higher in patients over 40 years of age and there was a 6% rise in carbapenem resistance [15]. On the other hand, one study observed that the most common isolates were *E. coli* (30%), *S. aureus* (21%), *K. pneumoniae* (18%), *P. aeruginosa* (10%), *A.baumannii* (8%) and *Enterococcus* sp. (5%) [19]. In a study from Chennai, MBL production was observed in 22% and ESBL production was observed in 56% of the gram-negative bacilli isolated. Out of all the organisms isolated, 9 were multidrug resistant (82%) [13]. Around 47% of mechanically ventilated COVID-19 patients developed ventilator-associated pneumonia with a predominant strain of multidrug-resistant *K. pneumonia* [16]. *E coli* were multidrug-resistant and sensitive only to tigecycline and colistin [11]. *Elizabethkingia* spp. was observed in 29% of all the non-fermenting gram-negative bacteria in Bloodstream infections; in a study from

Odisha [20]. These isolates showed good susceptibility to linezolid, vancomycin, chloramphenicol, ciprofloxacin, cefoperazone-sulbactam, and cotrimoxazole and poor susceptibility to gentamicin, amikacin, cefepime, imipenem, meropenem, ceftriaxone, ampicillin, and ceftazidime.

In COVID-19 patients from Rajasthan, Methicillin-resistant gram-positive isolates constituted 90% of cases, with a substantial level of resistance (70–90%) observed against macrolides, clindamycin, and quinolones. However, these isolates remained susceptible to gentamicin, cotrimoxazole, vancomycin, linezolid, and daptomycin [21]. A study conducted in Mysuru revealed that 62% of *S. aureus* isolates were identified as MRSA. All isolates were found to be susceptible to vancomycin, linezolid, and daptomycin while exhibiting resistance to oxacillin, trimethoprim/sulfamethoxazole, levofloxacin, ciprofloxacin, clindamycin, and erythromycin [21]. Khurana et al identified coagulase-negative *Staphylococcus aureus* (CoNS) in 12 out of 19 positive blood cultures of COVID-19 patients. And 4/12 was Methicillin-resistant CoNS and the rest were Methicillin-sensitive CoNS [12], but all were sensitive to vancomycin, teicoplanin, tigecycline, linezolid, and daptomycin. Another study from Karnataka observed that 36 of 123 COVID-19 patients in the ICU had a central line and 26% of them developed central line-associated bloodstream infection (CLABSI) with CoNS [16]. A study conducted in New Delhi revealed a higher prevalence of Gram-positive organisms (59%) compared to Gram-negative organisms (39%). Coagulase-negative *staphylococci* (CoNS) accounted for 32.8% of the bacterial isolates during the first wave, with *S. aureus* being the predominant gram-positive organism at 29.7%. Among these gram-positive microorganisms, 60.3% were identified as methicillin-resistant *Staphylococcus aureus* (MRSA). In contrast, during the second wave, *S. aureus* constituted 48.9% of the bacterial isolates, with 55% of these isolates being MRSA [17].

Discussion

The COVID-19 pandemic brought on unnecessary and overuse of antibiotics in the pretext of preventing secondary infections. This frequent use of antibiotics increased the antimicrobial resistance [22]. Studies reported that co-infections due to bacteria during the admission of COVID-19-positive patients were very low about 3-8% but the antibiotic use for the admitted patient is 50-75% [23]. Till November 2023, 6.9 million deaths were observed due to COVID-19 but data showed 0.7 million deaths were observed due to AMR per year. Though the rate of mortality of AMR was less when compared to that of COVID-19; the mortality rate for the former will keep increasing when compared with COVID-19. By 2050, the number of deaths due to AMR will rise to 10 million but the transmission of COVID-19 may be controlled in a few years [24]. In treating COVID-19, most of the antibiotics were ineffective but physicians prescribed the antibiotics for the suspected COVID-19 patients to minimize the bacterial coinfection, difficulty in ruling out the bacterial infections during the pandemic situation and to avoid the risk of bacterial superinfections. This reduced the death by a minimum but increased the AMR to a maximum [25]. COVID-19 patients with mild symptoms received various types of antibiotics including antiviral drugs, anthelmintics, macrolide antibiotics especially azithromycin and antimalarial drugs [26]. A systematic review on increased consumption of antibiotics during the COVID-19 pandemic stated that 78% of COVID-19 patients have been prescribed an antibiotic regardless of the severity of illness [3].

In this review, we scrutinized the findings of 12 studies that reported secondary infection and AMR during the COVID-19 pandemic in India. The most reported Gram-negative

bacteria present in the secondary infections are multidrug-resistant *A. baumannii, and K. pneumonia* followed by *E. coli*. *Acinetobacter* is listed as dangerous bacteria by WHO as it needs certain antibiotics for its treatment [27] *A. baumannii* is a motile aerobic organism that mostly causes infection in immunocompromised patients and the major reason for the outbreak of nosocomial infections by entering the host through ventilators, central line, and urinary catheters. When compared with other organisms like *P. aeruginosa* and *H. pylori* the adherence with mucosal layer property of *A. baumannii* was less but the organism was able to withstand dry environments and higher temperatures for prolonged periods [28]. Studies showed that secondary bacterial infections during Covid-19 were mostly due to *A. baumannii* and the mortality was also high with *A. baumannii* infections [29]. Chen et al, showed the presence of highly resistant *A. baumannii*in 1 of 99 patients admitted in China [30]. A study from Turkey reported that 8.7% of COVID-19 patients showed respiratory tract coinfection with bacteria. The predominant organisms were CoNS (31%), *A. baumannii* (27.5%), and *K. pneumonia* (9.5%). Among the three organisms, *A.baumanii* was resistant to the majority of antibiotics except for colistin and tigecycline [31]. A study from India reported that four isolates from COVID-19 patients were susceptible to colistin [18]. Similarly, a report from Iran also showed the incidence of *A. baumannii* was high in the COVID-19 patient. The study showed that 90% of the bacterial infection was due to *A. baumannii* 10% was *S. aureus* and among the 10% one was methicillin-resistant *S. aureus*. All the patients who showed superinfection with bacteria were dead. The bacteria were resistant to all the antibiotics except Colistin, but 52% of the *A. baumannii* showed resistance to colistin also. The study also showed the resistant pattern of *A.baumannii* was similar in discharged and deceased patients [32]. Most of the expired patients had one or more comorbidity but 2 patients died without comorbidities but only with *A. baumannii* coinfection. This year WHO has classified carbapenem-resistant *A. baumannii*in the critical group of bacterial priority pathogens list [33]. In this review, 2 studies have stated that 50% of *Acinetobacter spp.* were carbapenem-resistant. As the choices of antibiotics are limited for these resistant pathogens, healthcare workers and policymakers have a huge challenge ahead.

A retrospective study conducted in Wuhan reported coinfections in the COVID-19 cases were mainly due to *A. baumannii* and *K. pneumonia* and most of the infection was due to hospital-acquired pneumonia. Research from Saudi Arabia reported that *K. pneumoniae* was the predominant species identified in both ICU and non-ICU patients with SARS-CoV-2 infection [34]. The resistance rates of *K. pneumoniae* isolates were observed to exceed 90% for first-generation cephalosporins and over 80% for second and fourth generations, respectively [35]. The overreliance on antibiotics may have contributed to the selection and proliferation of drug-resistant strains of *K pneumoniae*, making infections harder to treat and potentially leading to higher mortality. Third-generation cephalosporins are used irrationally in our country for the general and pediatric population. According to WHO, 3rd-generation cephalosporin-resistant Enterobacterales fall into the critical group of pathogens [36]. Judicious use of antibiotics should be encouraged by the health providers. The emergence of multidrug-resistant Gram-negative bacteria, such as ESBL and MBL-producing strains has posed significant challenges to healthcare systems [13]. These bacteria, commonly found in the gut flora, are associated with various healthcare-associated infections, complicating the management of patients, especially those with severe COVID-19 cases requiring prolonged hospitalization

and intensive care. The overuse and misuse of antibiotics during the pandemic may contribute to the rise of antibiotic resistance in Gram-negative bacteria. This dual challenge of combating COVID-19 and managing infections caused by drug-resistant bacteria underscores the importance of prudent antibiotic use, infection control measures, and ongoing research efforts to address the evolving landscape of microbial resistance during these unprecedented times.

Bloodstream infections caused by multidrug-resistant *E. coli* were documented, with sensitivity limited to tigecycline and colistin [11]. Tigecycline serves as a last-resort medication for treating carbapenem-resistant Gram-negative bacterial infections [36]. Tigecycline combined with colistin has shown promising results against multidrug-resistant (MDR) *E. coli*. However, resistance to both these drugs has been reported in China [16]. Responsible use of these medications will ensure and prevent further development of antibiotic resistance.

Elizabethkingia spp are a group of non-fermenting gram-negative bacteria that typically inhabit the environment but can also cause opportunistic infections in humans, particularly in individuals with compromised immune systems or underlying health conditions. Sarathi et al reported multidrug-resistant *Elizabethkingia* spp and more than 75% were resistant to carbapenems, aminoglycosides, and third- and fourth-generation cephalosporin [20]. The extensive resistance to various β-lactams stems from the production of metallo-β-lactamases encoded by BlaB and Bla (GOB) genes, enabling the degradation of most β-lactam antibiotics [37]. Minocycline and piperacillin-tazobactam demonstrated 100% sensitivity [38]. Addressing the issue of antimicrobial resistance in *Elizabethkingia* spp is essential to ensure effective and timely interventions for affected patients and to mitigate the broader risks associated with antibiotic resistance in healthcare settings.

During the COVID-19 pandemic, private-sector healthcare facilities in the United States have witnessed a resurgence of Methicillin-resistant *S. aureus* (MRSA) hospital-onset infections, undoing all progress made over the past decade [39]. According to a recent document from WHO, MRSA is classified in the high group category [33]. In this review, four studies had seen an increase in MRSA [17, 19, 21] and high-level resistance in COVID-19-infected patients [11]. In India notable increase in MRSA was observed during COVID-19 infection and showed resistance to commonly used antibiotics like erythromycin, clindamycin, and fluoroquinolones [17]. In three studies, CoNS were the leading cause of bloodstream infections in COVID-19-infected patients [16, 17]. CoNS remain opportunistic pathogens, particularly concerning individuals with weakened immune systems or those utilizing indwelling medical devices like catheters or prosthetic implants. CoNS can lead to bloodstream infections, urinary tract infections, and issues related to implanted medical devices. Nonetheless, during the COVID-19 pandemic, vancomycin and linezolid demonstrated 100% susceptibility against gram-positive cocci [17].

A retrospective study conducted in the USA revealed elevated rates of mortality and extended hospital stays associated with inadequate empiric antibiotic therapy in both COVID-19 and non-COVID-19 patients [29]. The mortality rate and length of hospital stay were higher in COVID-19 patients who were given antibiotics [3]. It is believed that several healthcare-associated infections (HAIs), such as hospital/ventilator-associated pneumonia, bloodstream infections (BSIs), and urinary tract infections (UTIs), might be underreported due to limited culturing practices or the unavailability of culturing facilities in many hospitals [12]. Studies revealed that patients

with catheter-associated UTI had diabetes and chronic kidney disease, were on steroids and had a longer ICU stay; and patients with central line-associated bloodstream infection had more acute respiratory distress syndrome, had diabetes, were mechanically ventilated longer and had longer ICU stay [16]. The broad and excessive prescription of antibiotics may also be attributed to the fear and uncertainty surrounding the pandemic and the lack of antiviral therapies with shown efficacy [40]. In China, the use of broad-spectrum antibiotics especially respiratory quinolones was high in the initial stage of pandemics. COVID-19 brought many challenges socially, and economically, and in accessing treatment from healthcare centers including hospitals. There was a notable rise in antibiotic purchases, especially azithromycin, during the peak period of the initial COVID-19 outbreak in India. Similar patterns are expected in other low and middle-income nations where antibiotics are frequently overused [23]. A recent systematic review concluded that concerns related to COVID-19 and the lack of treatment strategy led to the overuse of antibiotics without proper clinical rationale [3]. The contributing factor to increased AMR during the COVID-19 pandemic might be to increased number of patients taking antimicrobials.

Though prescribing antibiotics in the pandemic situation was unavoidable, antibiotics should be given responsibly and frugally. Hunter et al, suggested antibiotics should be initiated only after testing for the sensitivity and resistant pattern of the organism, and when started, the treatment should be monitored [40]. Therefore early diagnosis and identification of bacterial infections along with antibiotic susceptibility testing and appropriate treatment would be ideal approaches to managing and reducing AMR.

Conclusion

The most common antimicrobial-resistant gram-negative bacteria were *A. baumanii, K. pneumonia* followed by *E. Coli* and the common gram-positive bacteria was *S aureus.* AMR during the COVID-19 pandemic was high. Preventing antimicrobial resistance is a multifaceted challenge that requires a comprehensive and coordinated approach. First and foremost, responsible and judicious use of antibiotics is crucial. Healthcare professionals should prescribe antibiotics only when necessary, and patients must complete their prescribed courses to ensure the complete eradication of the targeted infection. Public awareness campaigns are essential to educate individuals on the importance of proper antibiotic usage and the potential consequences of misuse. Improved hygiene practices, both in healthcare settings and in the community, can help reduce the spread of infections, thereby decreasing the need for antibiotic treatments. Additionally, fostering the development of new antibiotics and alternative treatment strategies is vital to combat emerging resistant strains. Collaborative efforts on a global scale, involving governments, healthcare providers, researchers, and the pharmaceutical industry, are essential to address antimicrobial resistance comprehensively and safeguard the effectiveness of existing and future antimicrobial treatments.

Conflict of Interest

The authors declare no conflict of interest.

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